REMARKS

Applicant respectfully request that the foregoing amendments to Claims and new Claims be entered in order to avoid this application incurring a surcharge for the presence of one or more multiple dependent claims.

Respectfully submitted,

Date April 16, 2001

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for/

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

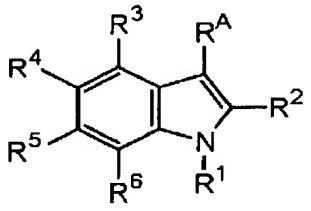
Amended Title:

[REMEDIES OR PREVENTIVES FOR ISCHEMIC REFLOW FAILURE]

COMPOSITION FOR TREATING OR PREVENTING ISCHEMIA REPERFUSION INJURY

32. (Amended) A preservation solution of claim 30 [or 31], wherein the $sPLA_2$ inhibitor is type-II PLA_2 inhibitor.

33. (Amended) A preservation solution of claim 30 [or 31], wherein the $sPLA_2$ inhibitor is a compound [of any one of claims 3 to 29] which contains a compound as an active ingredient, which is represented by the formula (I):



(I)

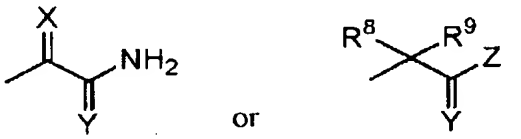
wherein R^1 is a group selected from (a) C7 to C20 alkyl, C7 to C20 alkenyl, C7 to C20 alkynyl, carbocyclic groups, and heterocyclic groups, (b) the groups represented by (a) each substituted independently with at least one group selected from non-interfering substituents, and (c) $-(L^1)-R^7$ wherein L^1 is a divalent linking group of 1 to 18 atom(s) selected from hydrogen atom(s), nitrogen atom(s), carbon atom(s), oxygen atom(s), and sulfur atom(s), wherein the combination atoms in L^1 are selected from the group consisting of i) carbon and hydrogen, ii) sulfur only, iii) oxygen only, iv) nitrogen and hydrogen only, v) carbon, hydrogen, and sulfer only, and vi) carbon, hydrogen, and oxygen only and R^7 is a group selected from the groups (a) and (b);

R^2 is hydrogen atom, halogen, C1 to C3 alkyl, C3 to C4 cycloalkyl, C3 to C4 cycloalkenyl, C1 to C3 alkyloxy, or C1 to C3 alkylthio;

R^3 and R^4 are each independently hydrogen atom, non-interfering substituents, or -(L^2)-(acidic group) wherein L^2 is an acid linker having an acid linker length of 1 to 5, provided that one of R^3 and R^4 is -(L^2)-(acidic group);

R^5 and R^6 are each independently hydrogen atom, non-interfering substituents, carbocyclic groups, carbocyclic groups substituted with a non-interfering substituent(s), heterocyclic groups, or heterocyclic groups substituted with a non-interfering substituent(s); and

R^A is a group represented by the formula:

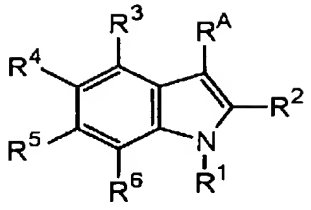


wherein R^8 and R^9 are each independently hydrogen atom, C1 to C3 alkyl or halogen; X and Y are each independently oxygen atom or sulfur atom; and Z is -NH_2 or -$NHNH_2$; the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.

34. (Amended) A preservation solution of [any one of] claim[s] 30, [to 33] wherein the organ is heart, liver, pancreas, kidney, or small intestine.

40. (Amended) A method for preventing ischemia reperfusion injury of [any one of] claim[s] 35 [to 39], wherein the $sPLA_2$ inhibitor is type-II PLA_2 inhibitor.

41. (Amended) A method for preventing ischemia reperfusion injury of [any one of claims 35 to 39] claim 35, wherein the $sPLA_2$ inhibitor is a compound [of any one of claims 3 to 29] which contains a compound as an active ingredient, which is represented by the formula (I):



(I)

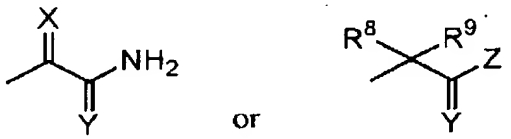
wherein R^1 is a group selected from (a) C7 to C20 alkyl, C7 to C20 alkenyl, C7 to C20 alkynyl, carbocyclic groups, and heterocyclic groups, (b) the groups represented by (a) each substituted independently with at least one group selected from non-interfering substituents, and (c) $-(L^1)-R^7$ wherein L^1 is a divalent linking group of 1 to 18 atom(s) selected from hydrogen atom(s), nitrogen atom(s), carbon atom(s), oxygen atom(s), and sulfur atom(s), wherein the combination atoms in L^1 are selected from the group consisting of i) carbon and hydrogen, ii) sulfur only, iii) oxygen only, iv) nitrogen and hydrogen only, v) carbon, hydrogen, and sulfer only, and vi) carbon, hydrogen, and oxygen only and R^7 is a group selected from the groups (a) and (b);

R^2 is hydrogen atom, halogen, C1 to C3 alkyl, C3 to C4 cycloalkyl, C3 to C4 cycloalkenyl, C1 to C3 alkyloxy, or C1 to C3 alkylthio;

R^3 and R^4 are each independently hydrogen atom, non-interfering substituents, or $-(L^2)-$(acidic group) wherein L^2 is an acid linker having an acid linker length of 1 to 5, provided that one of R^3 and R^4 is $-(L^2)-$(acidic group);

R^5 and R^6 are each independently hydrogen atom, non-interfering substituents, carbocyclic groups, carbocyclic groups substituted with a non-interfering substituent(s), heterocyclic groups, or heterocyclic groups substituted with a non-interfering substituent(s); and

R^A is a group represented by the formula:

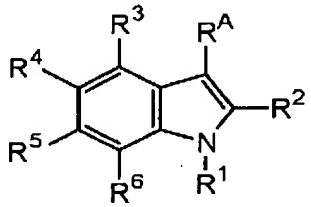


wherein R^8 and R^9 are each independently hydrogen atom, C1 to C3 alkyl or halogen; X and Y are each independently oxygen atom or sulfur atom; and Z is $-NH_2$ or $-NHNH_2$; the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.

42. (Amended) A method for preventing ischemia reperfusion injury of [any one of] claim[s] 37 [to 41], wherein the organ is heart, liver, pancreas, kidney, or small intestine.

47. (Amended) A method of treating ischemia reperfusion injury of [any one of] claim[s] 43 [to 46], wherein the $sPLA_2$ inhibitor is type-II PLA_2 inhibitor.

48. (Amended) A method of treating ischemia reperfusion injury of [any one of claims 43 to 46] claim 43, wherein the $sPLA_2$ inhibitor is a compound [of any one of claims 3 to 29] which contains a compound as an active ingredient, which is represented by the formula (I):



(I)

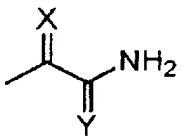
wherein R^1 is a group selected from (a) C7 to C20 alkyl, C7 to C20 alkenyl, C7 to C20 alkynyl, carbocyclic groups, and heterocyclic groups, (b) the groups represented by (a) each substituted independently with at least one group selected from non-interfering substituents, and (c) $-(L^1)-R^7$ wherein L^1 is a divalent linking group of 1 to 18 atom(s) selected from hydrogen atom(s), nitrogen atom(s), carbon atom(s), oxygen atom(s), and sulfur atom(s), wherein the combination atoms in L^1 are selected from the group consisting of i) carbon and hydrogen, ii) sulfur only, iii) oxygen only, iv) nitrogen and hydrogen only, v) carbon, hydrogen, and sulfer only, and vi) carbon, hydrogen, and oxygen only and R^7 is a group selected from the groups (a) and (b);

R^2 is hydrogen atom, halogen, C1 to C3 alkyl, C3 to C4 cycloalkyl, C3 to C4 cycloalkenyl, C1 to C3 alkyloxy, or C1 to C3 alkylthio;

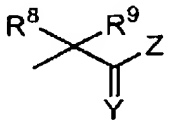
R^3 and R^4 are each independently hydrogen atom, non-interfering substituents, or -(L^2)-(acidic group) wherein L^2 is an acid linker having an acid linker length of 1 to 5, provided that one of R^3 and R^4 is -(L^2)-(acidic group);

R^5 and R^6 are each independently hydrogen atom, non-interfering substituents, carbocyclic groups, carbocyclic groups substituted with a non-interfering substituent(s), heterocyclic groups, or heterocyclic groups substituted with a non-interfering substituent(s); and

R^A is a group represented by the formula:



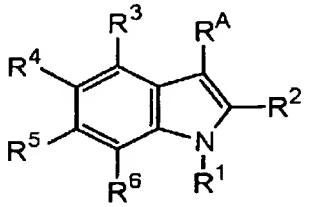
or



wherein R^8 and R^9 are each independently hydrogen atom, C1 to C3 alkyl or halogen; X and Y are each independently oxygen atom or sulfur atom; and Z is $-NH_2$ or $-NHNH_2$; the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.

49. (Amended) A method for treating ischemia reperfusion injury of [any one of] claim[s] 44 [to 48], wherein the organ is heart, liver, pancreas, kidney, or small intestine.

52. (Amended) A perservation method of claim 50, wherein the $sPLA_2$ inhibitor is a compound [of any one of claims 3 to 29] which contains a compound as an active ingredient, which is represented by the formula (I):



(I)

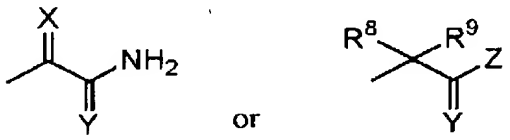
wherein R^1 is a group selected from (a) C7 to C20 alkyl, C7 to C20 alkenyl, C7 to C20 alkynyl, carbocyclic groups, and heterocyclic groups, (b) the groups represented by (a) each substituted independently with at least one group selected from non-interfering substituents, and (c) -(L^1)-R^7 wherein L^1 is a divalent linking group of 1 to 18 atom(s) selected from hydrogen atom(s), nitrogen atom(s), carbon atom(s), oxygen atom(s), and sulfur atom(s), wherein the combination atoms in L^1 are selected from the group consisting of i) carbon and hydrogen, ii) sulfur only, iii) oxygen only, iv) nitrogen and hydrogen only, v) carbon, hydrogen, and sulfer only, and vi) carbon, hydrogen, and oxygen only and R^7 is a group selected from the groups (a) and (b);

R^2 is hydrogen atom, halogen, C1 to C3 alkyl, C3 to C4 cycloalkyl, C3 to C4 cycloalkenyl, C1 to C3 alkyloxy, or C1 to C3 alkylthio;

R^3 and R^4 are each independently hydrogen atom, non-interfering substituents, or -(L^2)-(acidic group) wherein L^2 is an acid linker having an acid linker length of 1 to 5, provided that one of R^3 and R^4 is -(L^2)-(acidic group);

R^5 and R^6 are each independently hydrogen atom, non-interfering substituents, carbocyclic groups, carbocyclic groups substituted with a non-interfering substituent(s), heterocyclic groups, or heterocyclic groups substituted with a non-interfering substituent(s); and

R^A is a group represented by the formula:



wherein R^8 and R^9 are each independently hydrogen atom, C1 to C3 alkyl or halogen; X and Y are each independently oxygen atom or sulfur atom; and Z is -NH_2 or -$NHNH_2$; the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.